

	FR1	L1	FR2
			*
Murine	<u>DIOL</u> TQSPSSLA VSAGENVTF ^{**} SC	KSSQSVLYS ANHKNYLA	WYQQKPGQSP
REIHuVK	-----SA-V-DR-----	-----	-----KA-----
		FR3	L3
	L2	*	
Murine	<u>KLILY</u> WASTRES	GVPDRFTGSGSGTDEFTLTISRQVEDLA IYYC	HQYLSS
REIHuVK	-----	-----S--S-----F--SL-P-I-T-----	-----
		FR4	
	*		
Murine	<u>WTF</u>	<u>GGG</u> TKLEIKR	
REIHuVK	---	-----	

FIG. 1B

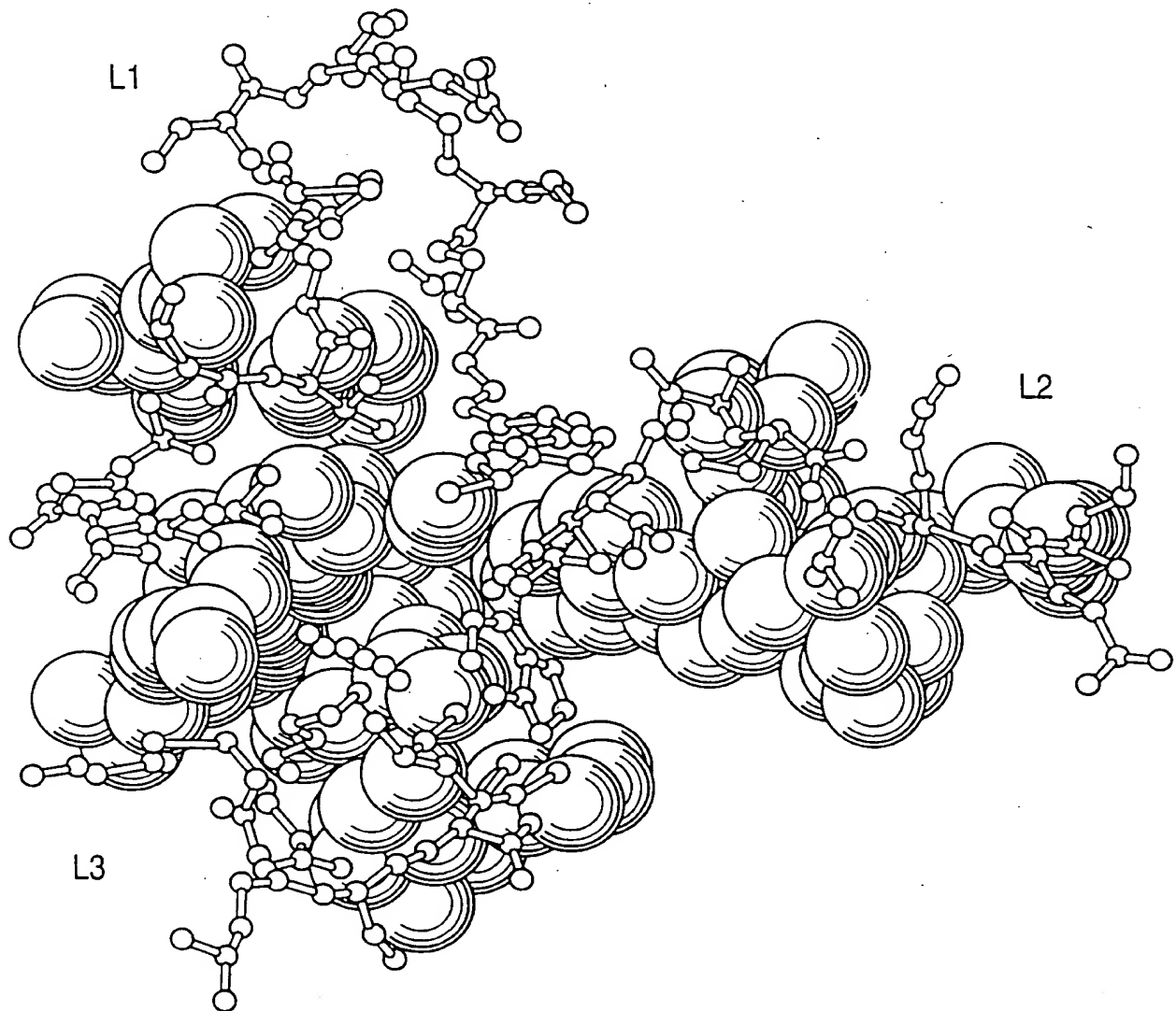
Murine EUHuVH1 EUHuVH2	FR1 QVQLQESGAELSKPGASVKMSCKASGYTFT -----Q-----VK-----S-----V----- -----VQ-----VK-----S-----V-----	H1 SYWLH ----- ----- -----	FR2 WIKQRPQGGLWIG -----VR-A----- -----VR-A-----	*
Murine EUHuVH1 EUHuVH2	H2 YINPRNDYTEYNQNFKD ----- -----	** KATLTADKSSSTAYMQLSSLTSED	FR3 SAVYYCAR -----I-----E-----R-----T-F-F----- -----I-----E-TN-----E-----R-----T-F-F-----	*
Murine NEWMHuVH1 NEWMHuVH2	H3 RDITTFY ----- -----	FR4 WGQGTTLTVSS -----V----- -----V-----		

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Appl. No.: 09/741,843

FIG. 2A



09741843-02001

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FIG. 2B

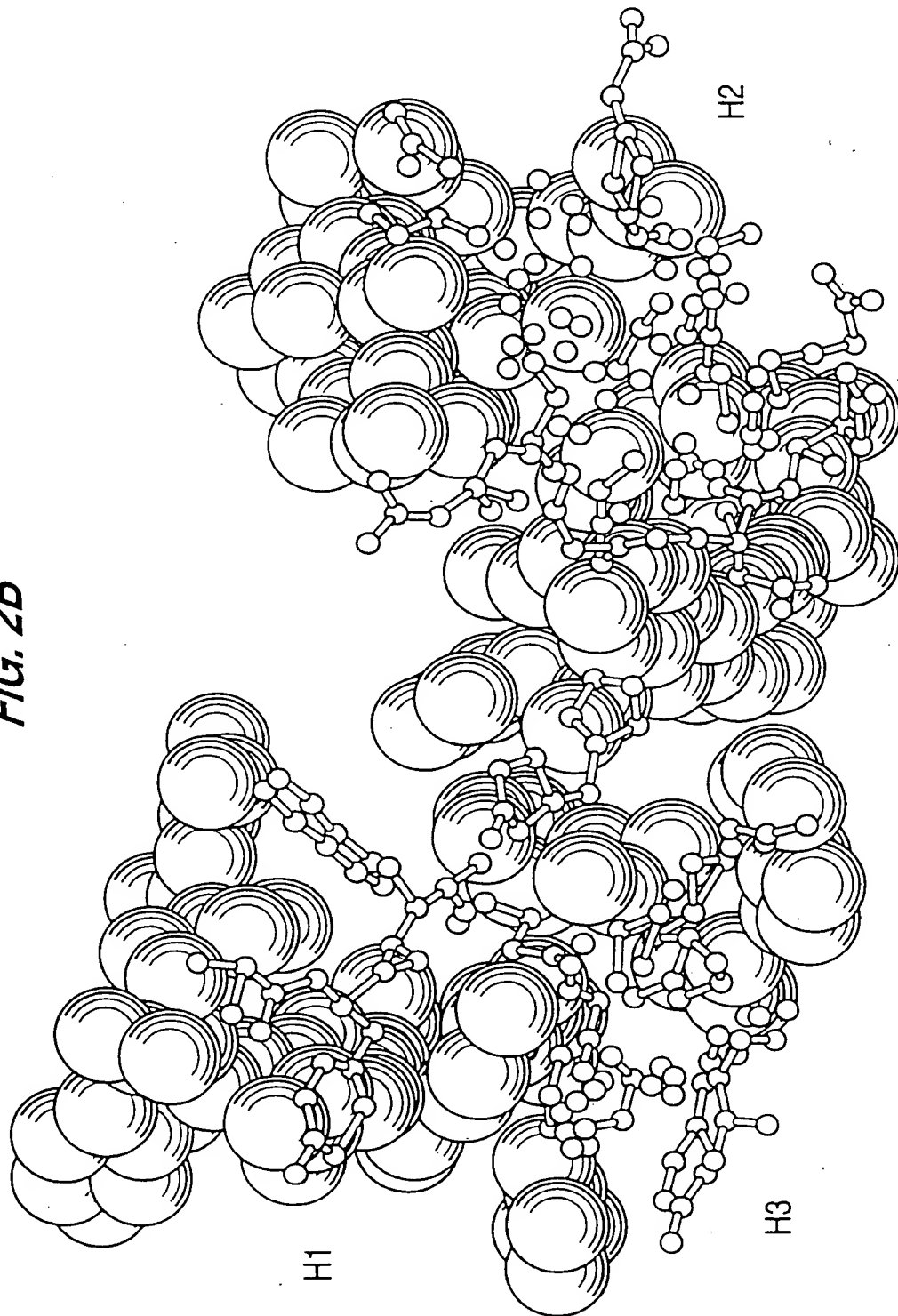


FIG. 2B

FIG. 3A

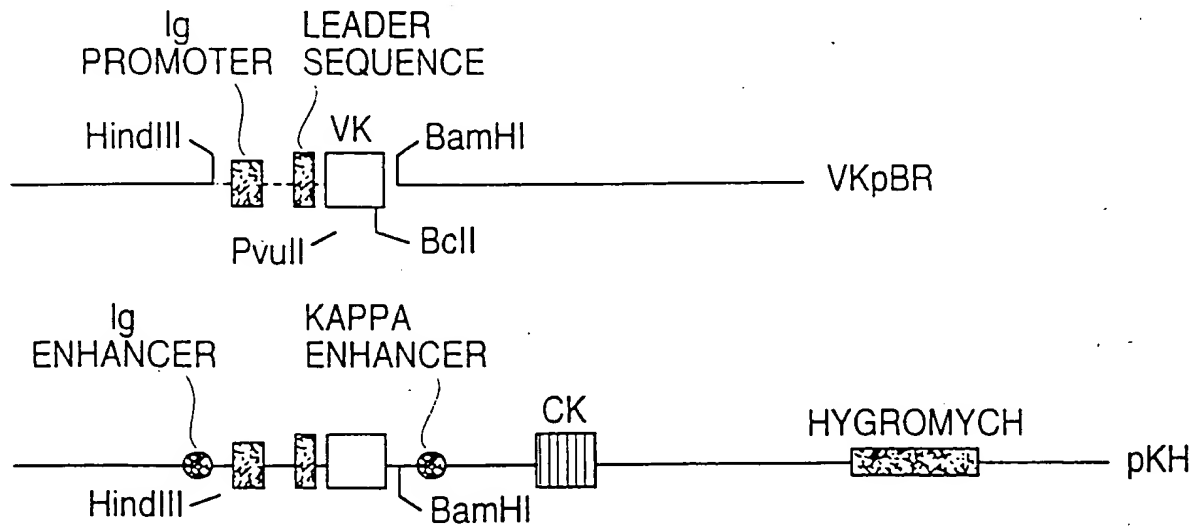
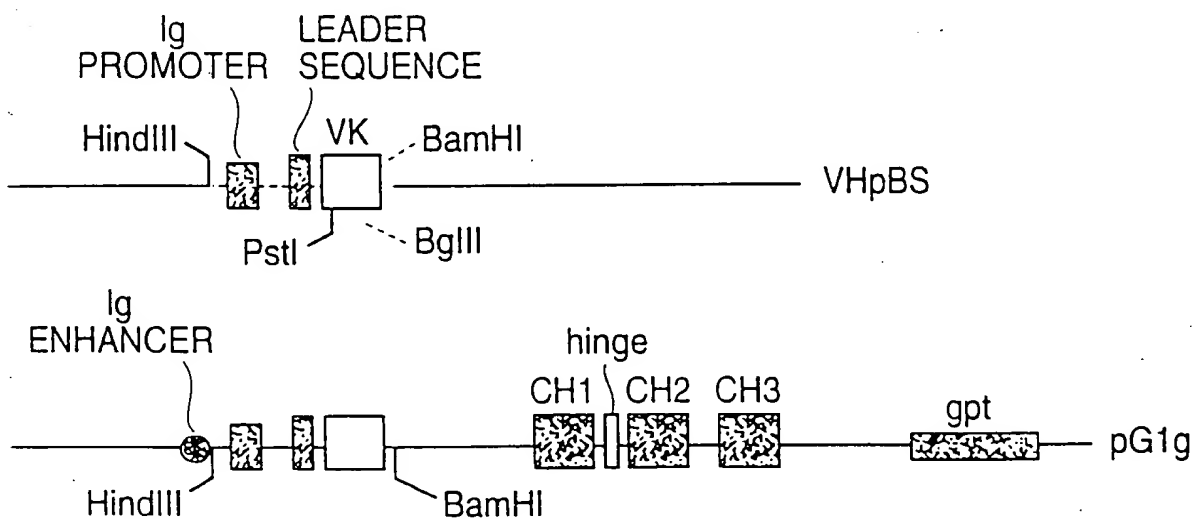


FIG. 3B



09741843-072001

FIG. 4A

FIG. 4A

```

GACATTCAGCTGACCCAGTCTCCATCATCTCTGGCTGTGTCTGCAGGAGAAAACGTCAC
1-----+-----+-----+-----+-----+-----+-----+-----+ 60
CTGTAAGTCGACTGGGTCAGAGGTTAGAGACCGACACAGACGTCCTCTTTTGCAGTGA

D I Q L T Q S P S L A V S A G E N V T
ATGAGCTGTAAGTCCAGTCAAAGTGTTTATACAGTGCAAAATCACAGAAGTACTTGGCC
61-----+-----+-----+-----+-----+-----+-----+-----+ 120
TACTCGACATTCAGGTCAGTTTCACAAAATATGTCACGTTTAGTGTTCTTGATGAACCGG

                                CDR1
M S C [K S S Q S V L Y S A N H K N Y L A]
TGGTACCAGCAGAAACCAGGGCAGTCTCTCTAACTGCTGATCTACTGGGCATCCACTAGG
121-----+-----+-----+-----+-----+-----+-----+-----+ 180
ACCATGGTCGCTTTGGTCCCGTCAGAGGATTTGACGACTAGATGACCCGTAGGTGATCC

                                CDR2
W Y Q Q K P G Q S P K L L I Y [W A S T R]
GAATCTGTGTCCTGATCGCTTCACAGGCAGCGGATCTGGACAGATTTACTCTTACC
181-----+-----+-----+-----+-----+-----+-----+-----+ 240
CTTAGACCACAGGGACTAGCGAAGTGTCGTCGCTAGACCCCTGTCTAAATGAGAATGG

[E S] G V P D R F T G S G S G T D F T L T
ATCAGCAGAGTACAAGTTGAAGACCTGGCAATTATTATTGTCACCAATACCTCTCCTCG
241-----+-----+-----+-----+-----+-----+-----+-----+ 300
TAGTCGTCTCATGTTCAACTTCTGGACCGTTAAATAATAACAGTGGTTATGGAGAGGAGC

                                CDR3
I S R V Q V E D L A I Y Y C [H Q Y L S S]
TGGACGTTTCGGTGGAGGGACCAAGCTGGAGATCAAAACGT
301-----+-----+-----+-----+-----+-----+-----+-----+ 339
ACCTGCAAGCCACCTCCCTGGTTCGACCTCTAGTTGCA
[W T F] G G G T K L E I K R -

```

FIG. 4B

CAGGTCAGCTGCAGGAGTCAGGGGCTGAACTGTCAAAACCTGGGGCCTCAGTGAAGATG
 1 -----+-----+-----+-----+-----+ 60
 GTCCAGGTCGACGTCCTCAGTCCCCGACTTGACAGTTTGGACCCCGGAGTCACTTCTAC
 Q V Q L Q E S G A E L S K P G A S V K M -
 TCCTGCAAGGCTTCTGGCTACACCTTTACTAGTACTGGCTGCACTGGATAAAACAGAGG
 61 -----+-----+-----+-----+-----+ 120
 AGGACGTTCCGAAGACCGATGTGGAAATGATCGATGACCGACGTGACCTATTTTGTCTCC
 S C K A S G Y T F T [S Y W L H] W I K Q R -
 CDR1
 CCTGACAGGTCCTGGAATGGATTGGATACATTAATCCTAGGAATGATTATACTAGTAC
 121 -----+-----+-----+-----+-----+ 180
 GGACCTGTCCCAGACCTTACCTAACCTATGTAATAGGATCCTTACTAATATGACTCATG
 CDR2
 P G Q G L E W I G [Y I N P R N D Y T E Y] -
 AATCAGAACTTCAAGGACAAGGCCACATTTGACTGCAGACAAATCCTCCAGCACAGCCTAC
 181 -----+-----+-----+-----+-----+ 240
 TTAGTCTTGAAGTCCCTGTTCCGGTGTAAGTACGTCGTCGTTAGGAGGTCGTGTCGGATG
 [N Q N F K D] K A T L T A D K S S T A Y -
 ATGCAACTGAGCAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGAGGAT
 241 -----+-----+-----+-----+-----+ 300
 TACGTTGACTCGTCGGACTGTAGACTCCTGAGACGTCAGATAATGACACGTTCTTCCCTA
 M Q L S S L T S E D S A V Y Y C A R [R D] -
 ATTACTACGTTCTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCG
 301 -----+-----+-----+-----+-----+ 348
 TAATGATGCAAGATGACCCCGGTTCCGGTGGTGAGAGTGTGAGAGGAGC
 CDR3
 [I T T F Y] W G Q G T T L T V S S -

FIG. 5A

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Appl. No.: 09/741,843

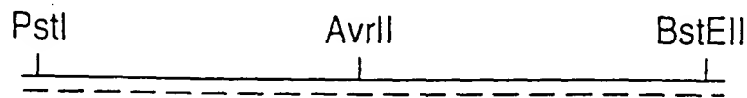
FIG. 5B

FIG. 5B

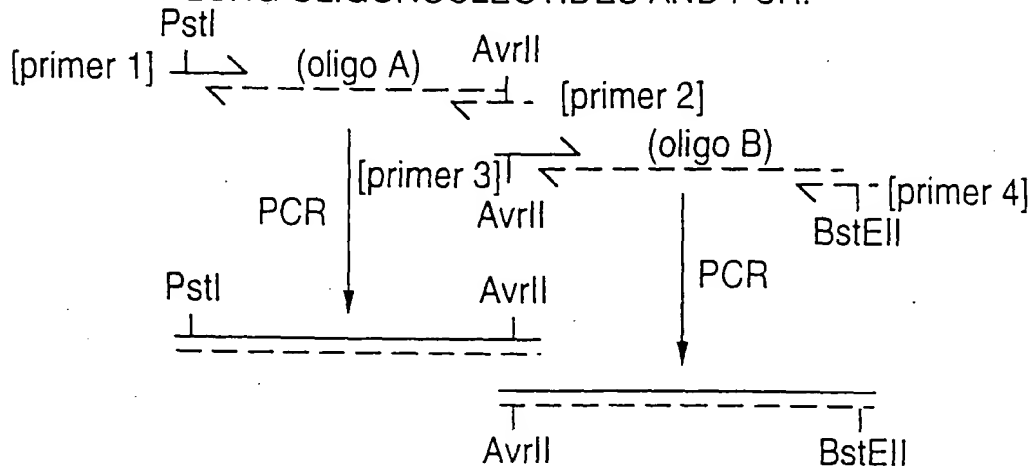
CAGGTCCAGCTGGTCCAATCAGGGGCTGAAGTCAAGAAACCTGGGTCAATCAGTGAAGGTC
 1-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 60
 GTCCAGGTCCGACCAAGGTTAGTCCCCGACTTCAGTTCTTTGGACCCAGTAGTCACTTCCAG
 Q V Q L V Q S G A E V K K P G S S V K V -
 TCCTGCAAGGCTTCTGGCTACACCTTTACTAGTACTGGCTGCACCTGGGTCAAGGCAGGCA
 61-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 120
 AGGACGTTCCGAAGACCGATGTGGAAATGATCGATGACCGACGTGACCCAGTCCCGTCCGT
 CDR1
 S C K A S G Y T F T [S Y W L H] W V R Q A -
 CCTGGACAGGGTCTGGAATGGATGGATACATTAATCCTAGGAATGATTATCTAGTAC
 121-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 180
 GGACCTGTCCCAGACCTTACCTAACCTATGTAATTAGGATCCTTACTAATAATGACTCATG
 CDR2
 P G Q G L E W I G Y I N P R N D Y T E Y -
 AATCAGAACTTCAAGGACAAGGCCACAATAACTGCAGACGAATCCACCAATACAGCCTAC
 181-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 240
 TTAGTCTTGAAGTTCCCTGTTCCGGTGTTATTGACGCTCTGCTTAGGTGGTTATGTCGGATG
 [N Q N F K D] K A T I T A D E S T N T A Y -
 ATGGAGCTGAGCAGCCTGAGGTCTGAGGACACGGCATTTTATTTTGTGCAAGAGGGAT
 241-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 300
 TACCTCGACTCGTCGGACTCCAGACTCCTGTGCCGTAAATAAACAACACGTTCTTCCCTA
 M E L S S L R S E D T A F Y F C A R [R D] -
 ATTACTACGTTCTACTGGGGCCAAGCACCACGGTCACCGTCTCCTCG
 301-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 348
 TAATGATGCAAGATGACCCCGGTTCCGTGTCGCCAGTGGCAGAGGAGC
 CDR3
 [I T T F Y] W G Q G T T V T V S S -

FIG. 6

DESIGNED SEQUENCE FOR HUMANIZED LL2 VH DOMAIN:



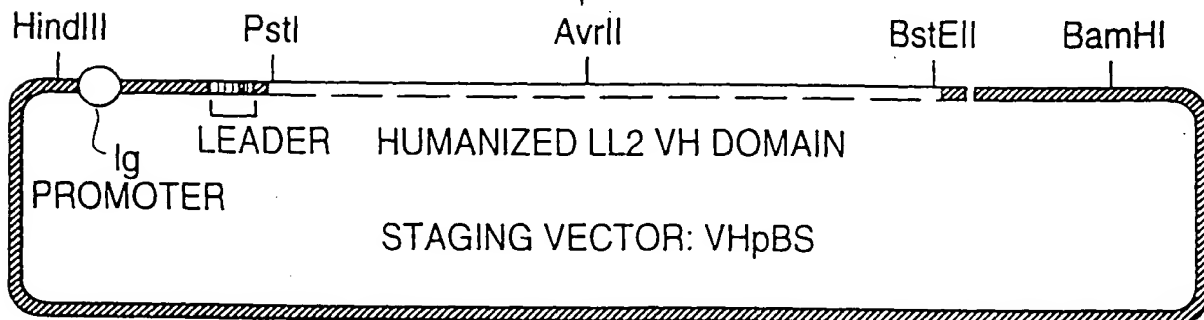
CONSTRUCTION OF THE HUMANIZED LL2 VH DOMAIN
BY LONG OLIGONUCLEOTIDES AND PCR:



PstI/AvrII DIGESTION

BstEII/AvrII DIGESTION

LIGATION TO THE PstI/BstEII
SITES OF THE HEAVY CHAIN
STAGING VECTOR: VHpBS



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FIG. 7

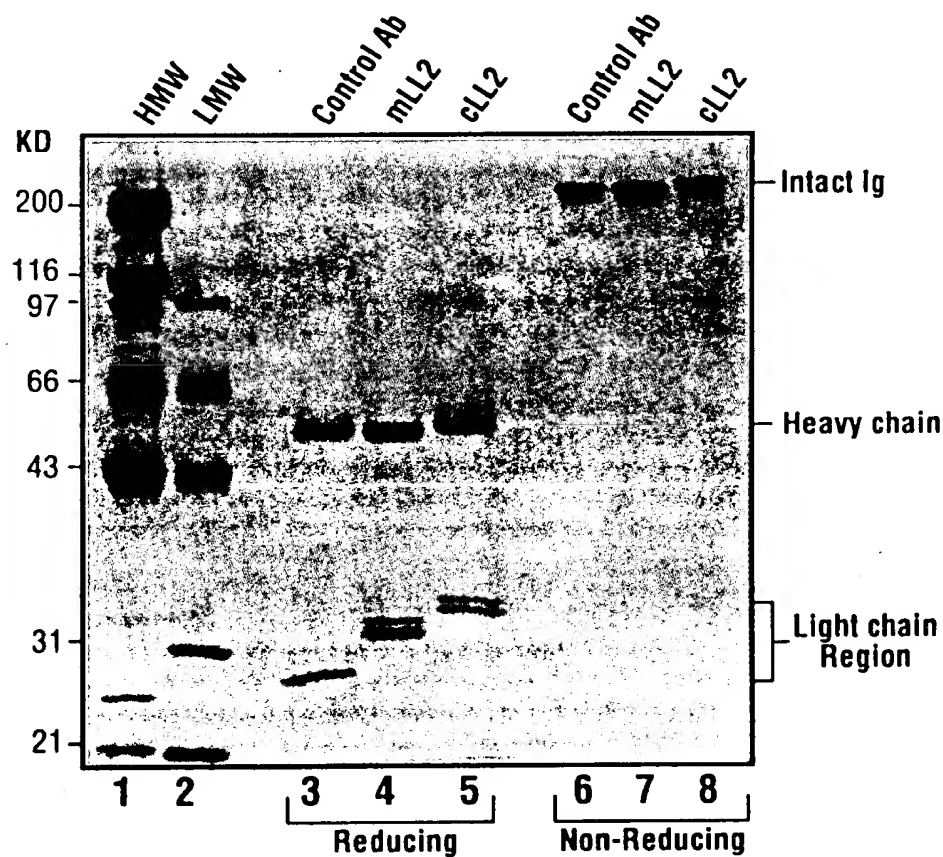


FIG. 8

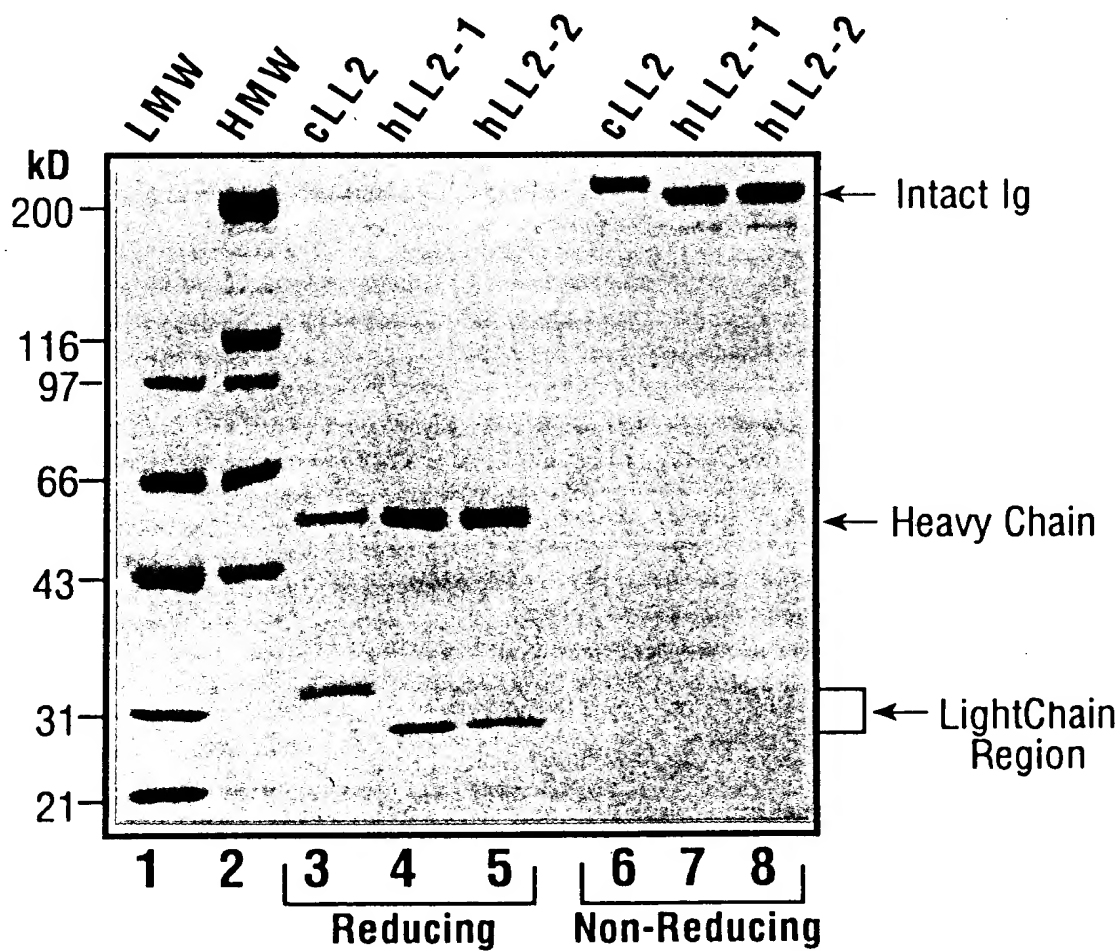


FIG. 9

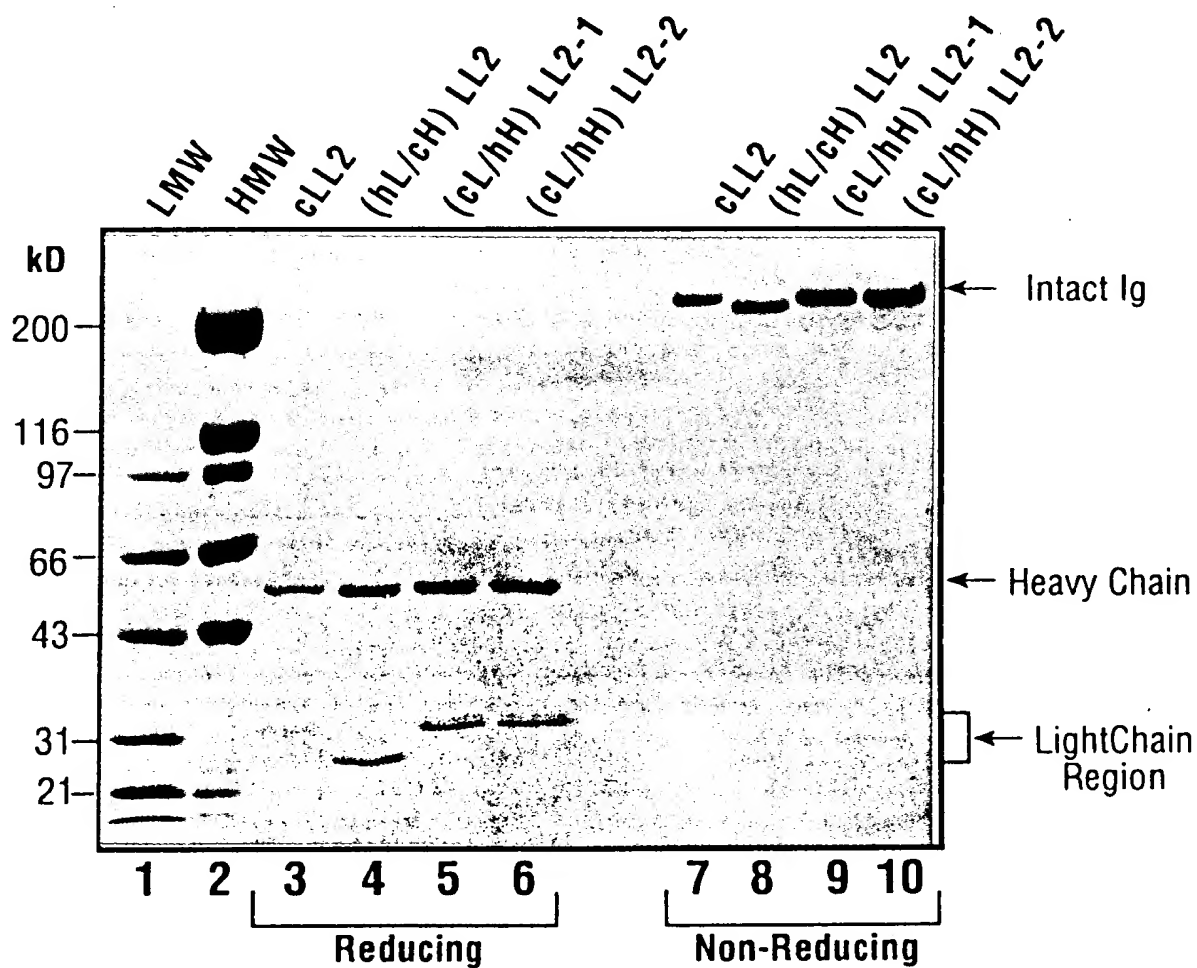


FIG. 10

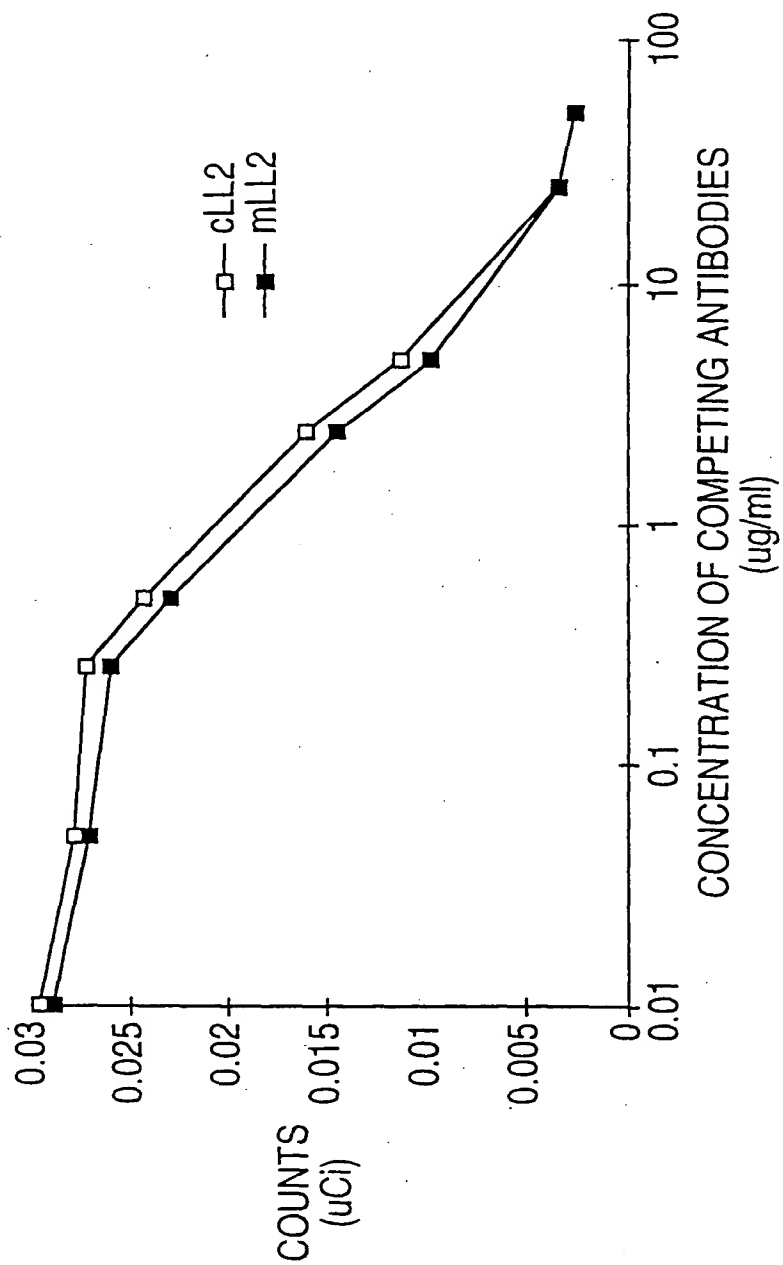


FIG. 11A

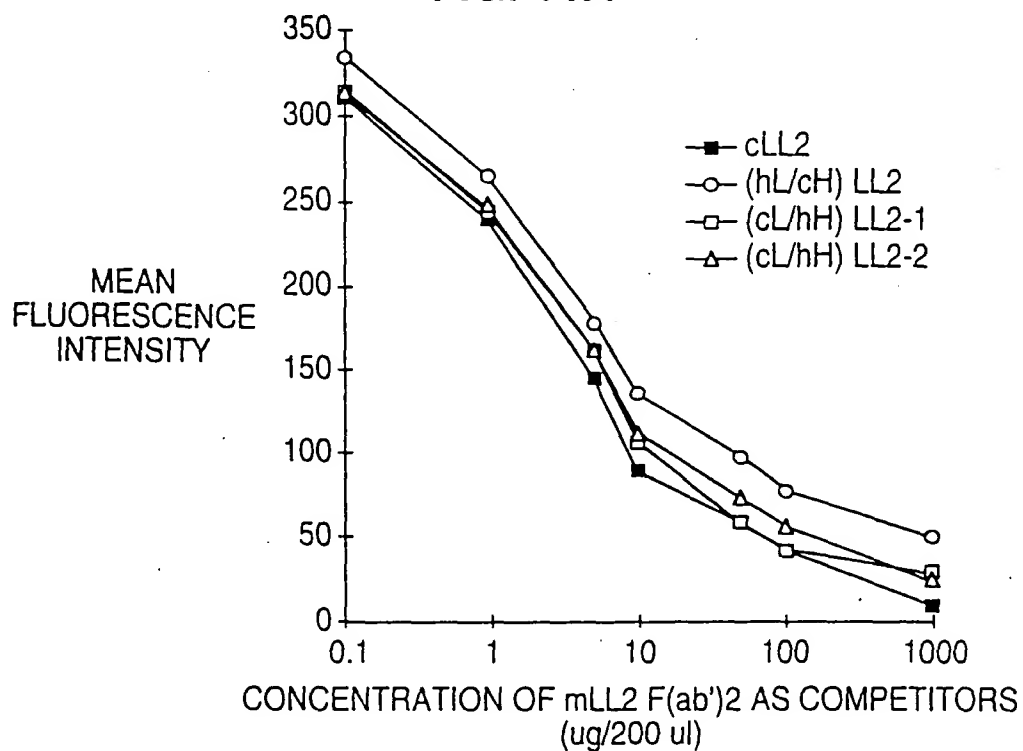


FIG. 11B

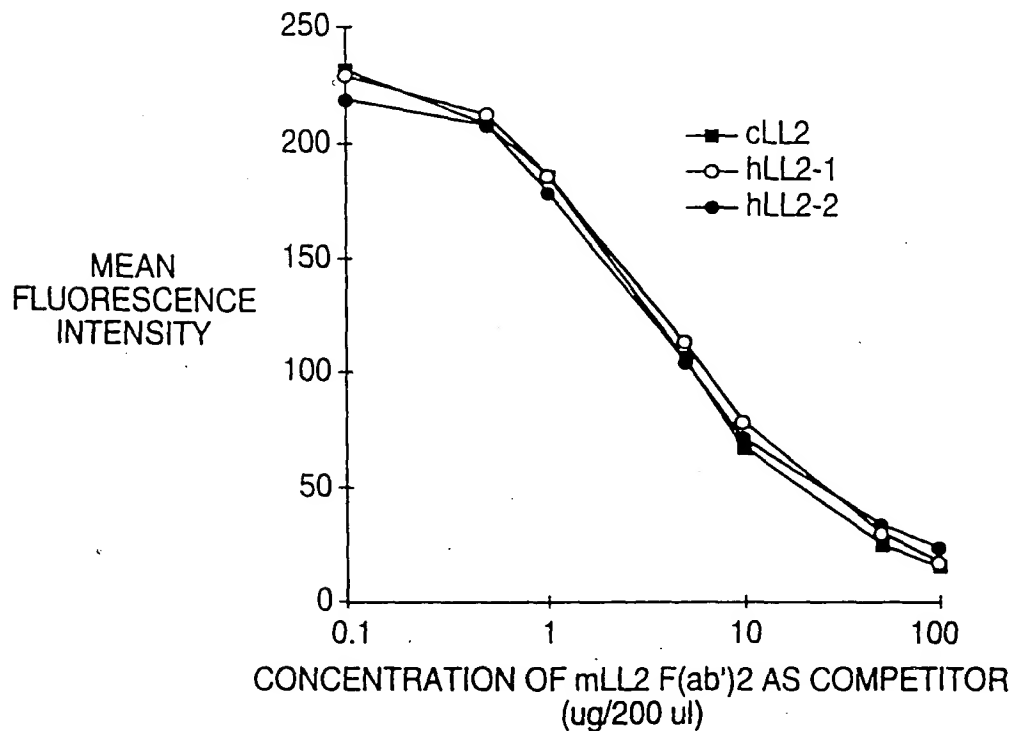


FIG. 12

INTERNALIZATION: c-LL2, h-LL2 vs. m-LL2 IN RAJI CELLS

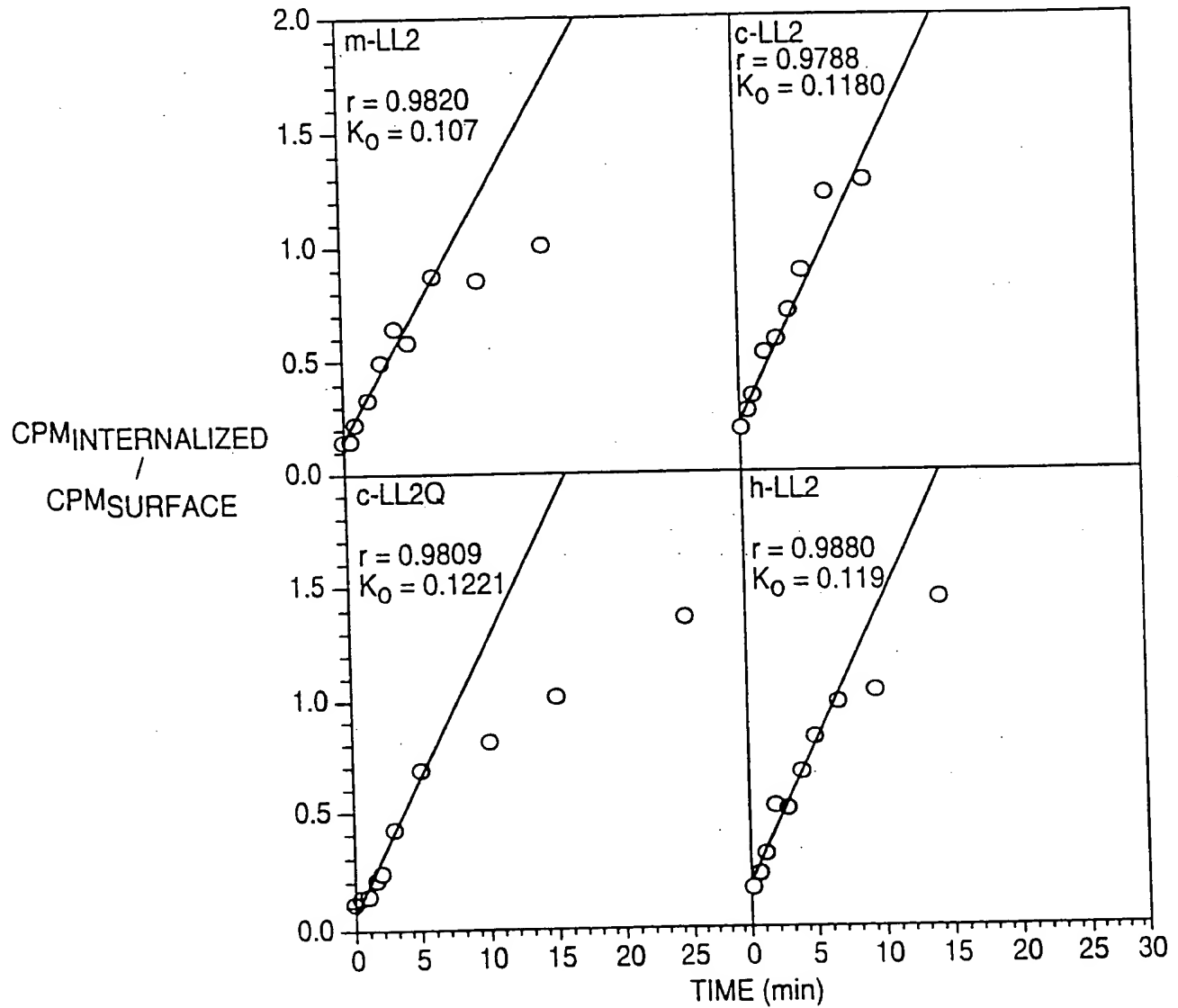
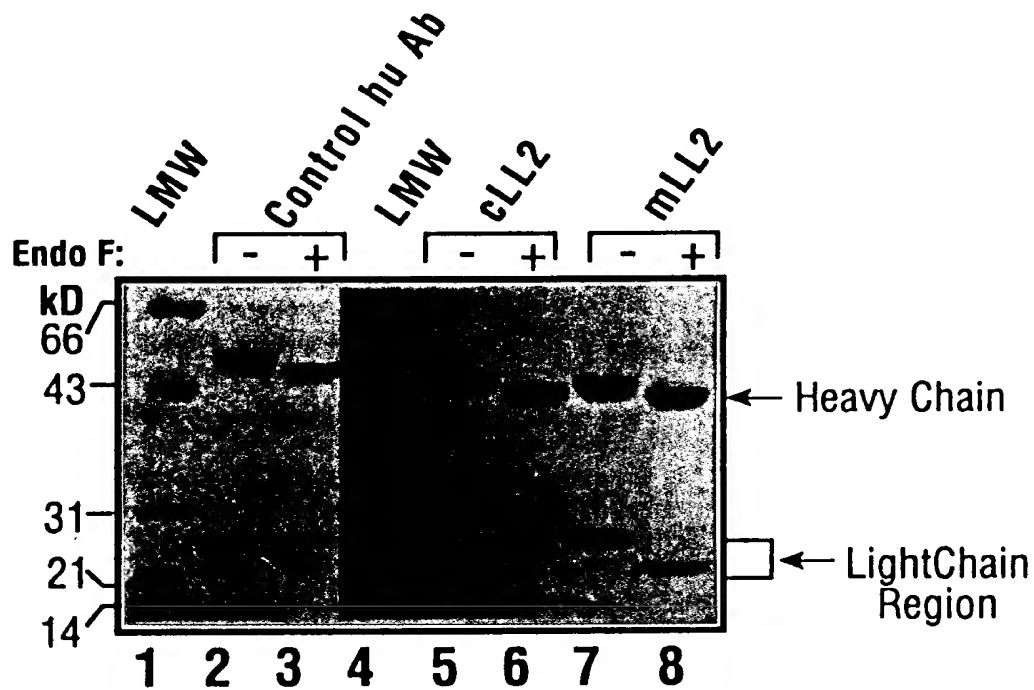


FIG. 13



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FIG. 14

